

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AFFYMETRIX, INC.,

Plaintiff/Counter-
Defendant,

v.

ILLUMINA, INC.,

Defendant/Counter-
Plaintiff.

C.A. No. 04-901-JJF

REDACTED VERSION

**PLAINTIFF AFFYMETRIX, INC.'S STATEMENT OF DISPUTED MATERIAL FACTS
IN RESPONSE TO ILLUMINA, INC.'S MOTION FOR SUMMARY JUDGMENT OF
INVALIDITY OF THE ASSERTED CLAIMS OF THE '432 PATENT**

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INTRODUCTION

1. Pursuant to this Court's Memorandum Order on Summary Judgment Procedure, Plaintiff Affymetrix, Inc. ("Affymetrix") submits this counterstatement of disputed facts in opposition to Illumina's Motion for Summary Judgment of Invalidity of the Asserted Claims of the '432 Patent, D.I. 279.

2. In its motion and supporting memorandum, Illumina seeks summary judgment that asserted claims 2, 5, 8, and 9 of U.S. Patent No. 6,355,432¹ (Exh. 1) are invalid under § 102(b) as anticipated by a minimal (less than one page) poster abstract entitled "Miniaturization of Sequencing By Hybridization (SBH): A Novel Method for Genome Sequencing." (Exh. 2, "the SBH Abstract"). The SBH Abstract lists as its authors four Yugoslavian scientists, including two that have been deposed in this case, Dr. Radomir Crkvenjakov and Dr. Radoje Drmanac.

3. In seeking to invalidate the claims of a patent, Illumina bears the burden of establishing invalidity by clear and convincing evidence. *See Avia Group Int'l., Inc. v. L.A. Gear Cal., Inc.*, 853 F.2d 1557, 1562 (Fed. Cir. 1988) ("[A] challenger must establish facts, by clear and convincing evidence, which persuasively lead to the conclusion of invalidity.").

4. Section 102(b) provides:

A person shall be entitled to a patent unless . . . (b) the invention was patented or described in a printed publication in this or a

¹ Illumina does not move for summary judgment with regard to claims 10, 21, and 22 of the '432 patent. As Affymetrix informed the Court, these claims were added to the asserted claims after a delay of relevant discovery by Illumina (including a delay of the most relevant deposition, the Rule 30(b)(6) deposition regarding Illumina's commercial products). These claims include limitations requiring at least 100,000 different sequences (claim 10), that the beads be reusable (claim 21), and that the oligonucleotides attached to the beads have different lengths (claim 22). These claims are also not anticipated by the SBH Abstract, for the reasons discussed in this brief and additional reasons.

foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States.

35 U.S.C. § 102(b). To anticipate a claim for purposes of § 102(b), a reference must have been publicly accessible at the time of the invention. *See In re Cronyn*, 890 F.2d 1158, 1160 (Fed. Cir. 1989). Section 102(b) also requires that the reference disclose all of the elements of the claim in sufficient detail to enable one of skill in the art to make the claimed invention without engaging in undue experimentation. *See Helifix Ltd. v. Blok-Lok, Ltd.*, 208 F.3d 1339, 1348 (Fed. Cir. 2000); *Biogen, Inc. v. Amgen, Inc.*, 973 F. Supp. 39, 42 (D. Mass. 1997) (denying summary judgment of anticipation where moving party failed to establish that scientific abstract was enabling). What a reference discloses and whether undue experimentation would be required to make a disclosed invention are questions of fact. *See Rockwell Int'l. Corp. v. United States*, 147 F.3d 1358, 1364 (Fed. Cir. 1998); *Biogen*, 973 F. Supp. at 43.

5. Illumina has submitted no expert testimony in support of its motion, despite moving for summary judgment on grounds that necessitate extensive factual inquiries that are the subject of expert testimony. By contrast, Affymetrix submits herewith the Declaration of Dr. Hubert Köster, a renowned expert in technologies such as chemical synthesis of DNA and genomics. (See Exh. 3).

6. Disputed issues of fact exist with respect to at least three aspects of Illumina's motion. First, there are disputed issues of fact with respect to whether the SBH Abstract discloses "an encoding system whereby the target specific sequence of the polymer attached to the beads can be identified." Second, there are disputed issues of fact regarding whether the SBH Abstract would enable one of skill in the art to make the claimed invention. Third, there are disputed issues of fact with regard to whether the SBH Abstract is a "printed publication" for purposes of § 102(b).

7. Illumina relies solely on attorney argument and citations to the deposition testimony of selected third parties in support of its Motion. These parties include two of the authors of the SBH Abstract, Drs. Crkvenjakov and Drmanac, the Department of Energy grant referee who funded their research, Marvin Stodolsky (Exh. 4, Stodolsky Depo. at 16:11-14), and a former collaborator and business partner, Kenneth Beattie (Exh. 5, Beattie Depo. at 88:6-24), all of whom had an interest in the success of Dr. Drmanac and Crkvenjakov's ideas, and all of whom were familiar with their theories from private communications and later developments – not only from the four corners of the document or any other information publicly accessible as of Affymetrix's priority date.

8. Drs. Drmanac and Crkvenjakov were involved in a previous litigation against Affymetrix in connection with their former company, "Hyseq." (Exh. 6, Crkvenjakov Depo. at 12:2-11; Exh. 7, Drmanac Depo. at 10:11-12). Additionally, as Illumina acknowledges in a footnote, Dr. Crkvenjakov is a paid consultant for Illumina for purposes of this litigation².

ARGUMENT

I. DISPUTED ISSUES OF FACT EXIST REGARDING WHETHER THE SBH ABSTRACT ADEQUATELY DISCLOSES ALL OF THE LIMITATIONS OF THE ASSERTED CLAIMS

9. Claim 2 of the '432 patent is dependent on claim 1, and claims 5, 8 and 9 are dependent on claim 2. Claim 1 reads:

A collection of beads comprising a plurality of beads which have binding polymers of different target specific sequence attached thereto; said beads being coded with an encoding system whereby

² Illumina also cites to the testimony of Dr. Richard Mathies. During his deposition, Dr. Mathies referred to Drs. Crkvenjakov and Drmanac as (Exh. 8, Mathies Depo. at 11:23.)

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the target specific sequence of the polymer attached to the beads can be identified.

‘432 Patent at col. 82, ll. 51-55. Claim 2 requires that the “polymer attached to the beads” described in claim 1 “is an oligonucleotide of a given length and is selected from the group consisting of all possible oligonucleotide sequences having the same number of nucleotides.” *Id.* at col. 82, ll. 56-59. Claims 5 and 8 require that the nucleotide sequences of uniform length are at least 5 and 10 nucleotides long, respectively. *See id.* at col. 83, ll. 1-3, 10-12. Claim 9 requires that “at least 10,000 of all the possible oligonucleotide sequences having the same number of nucleotides are each attached to a different single bead.” *Id.* at col. 83, ll. 13-16.

10. The person of ordinary skill in the art would not understand the SBH Abstract to disclose the claimed collection of beads “with an encoding system whereby the target specific sequence of the [oligonucleotide] attached to the beads can be identified” as required by all of the asserted claims. In fact, the SBH Abstract does not “disclose” any material invention, whatsoever. Rather, the SBH Abstract is, as Illumina’s nomenclature suggests, an “abstract” – it provides at most a sketch of a theoretical method by which the “Sequencing by Hybridization” (also “SbH” or “SBH”) methodology, imagined as a strategy for sequencing the human genome, might possibly be implemented in a “miniaturized” form, without disclosing key aspects of that implementation.

the proposed system was never built, at any scale:

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the “Sequencing by Hybridization” scheme advanced by the Yugoslavian scientists in this abstract in 1989 has never been implemented still 17 years later in 2006:

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11. Illumina states that “the [SBH] Abstract describes how the attached sequence can be identified by its association with a ‘premarked’ or encoded bead.” (Illumina Br. at 13). This interpretation of the Abstract is inaccurate. The SBH Abstract does not “describe” any functioning system or technical details. It merely states that, in theory, one could determine a sequence attached to a given bead given an index linking observable attributes of the beads to the attached sequences.³ This (tautological) idea follows from the general theory of SBH that posits that an unknown sequence might be assembled by overlapping short stretches of known sequence; namely, oligonucleotides that are found to hybridize to a polynucleotide of unknown target sequence. One needs to know which specific oligonucleotides bind to the target sequence to have anything to “assemble.” Illumina wishes to pull up this theoretical consideration by its figurative bootstraps and turn it into a “disclosure” of an actual “encoding system whereby the target specific sequence of the polymer can be identified” – a working system. Such a reading would essentially render the limitation meaningless, however. Because the SBH Abstract does not disclose all of the limitations of any of the asserted claims, it cannot anticipate those claims.

³ Illumina repeatedly makes statements in its brief such as “. . .the SBH Abstract *demonstrates* how over 10 million different beads, each attached with a different oligonucleotide of 12 to 15 nucleotides (i.e., a “12-15mer”)” (Br. at 5) and “. . .the SBH Abstract *demonstrates* a collection of beads with oligonucleotides attached. . .” (Br. at 7) implying that scientists would read the SBH Abstract to show proof of principle. These statements are imprecise and inaccurate. To be clear: *The SBH Abstract “demonstrates” nothing* – no such apparatus was ever built, despite Illumina’s persistent use of language that suggests otherwise.

12. The asserted claims require that oligonucleotides of known length be attached to beads, and that the sequence of the oligonucleotide attached to a given bead be determinable. Although the means by which one bead can be distinguished from another bead – by color, by shape, or by size – are mentioned in the SBH Abstract, there is *no* discussion of the technical details necessary to allow the bead attribute to facilitate determination of the actual *sequence* of the oligonucleotide attached to the bead with that attribute, as required by the asserted claims of the '432 patent. For example, there is no disclosure of any means of specific synthesis or attachment that would facilitate the construction of encoded DPs with different known sequences attached. In other words, for a system to meet the limitations of the claims of the '432 patent, it is not enough for it to allow one to be able to tell one bead from another bead. One must also be able to determine the sequence of the oligonucleotide attached to each bead without losing the bead identification information. As Dr. Köster will testify, at the time of the Abstract's alleged submission, there existed technical obstacles to constructing such a system, and the SBH Abstract offers no guidance to one of skill in the art toward overcoming them.

II. DISPUTED ISSUES OF FACT EXIST REGARDING WHETHER THE SBH ABSTRACT IS AN ENABLING DISCLOSURE

13. For a reference to "describe" the elements of a later claim, it must enable one of skill in the art to make the invention without "undue experimentation." *See Reading & Bates Constr. Co. v. Baker Energy Res. Corp.*, 748 F.2d 645, 651 (Fed. Cir. 1984). Whether "undue experimentation" would be required to make an invention disclosed in a printed publication requires inquiry into a number of factual questions, such as:

- (1) The quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the

predictability or unpredictability of the art, and (8) the breadth of the claims.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988) (discussing “undue experimentation” in the context of the § 112 enablement requirement); *See Elan Pharm., Inc. v. Mayo Found. for Med. Educ. & Research*, 346 F.3d 1051, 1055 (Fed. Cir. 2003) (applying *Wands* factors to determine enablement of a prior art reference).

14. A highly fact-intensive inquiry into issues such as whether undue experimentation would be required to practice an invention typically requires the aid of expert testimony, and disagreement among experts is sufficient to create an issue of material fact. *See Scanner Techs. Corp. v. Icos Vision Sys. Corp., N.V.*, 253 F. Supp. 2d 624, 636 (S.D.N.Y. 2003) (denying summary judgment on enablement where expert witnesses disagreed).

15. Illumina impermissibly seeks to elevate “the mere germ of an idea” to the status of an *invention*. *Genentech v. Novo Nordisk*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). That the SBH Abstract is not enabling is evident from the Abstract itself and the deposition testimony taken in this case. The final sentence of the SBH Abstract states, “[t]he described miniaturization concept and ensuing savings make human genome sequencing immediately feasible in a laboratory *pending technological development.*” SBH Abstract at ll. 42-45 (emphasis added). 17 years later, we still await this “technological development.” *Supra*, pp 4-5. Thus, the SBH Abstract itself, which purports to describe a theoretical method for sequencing the entire human genome, states that its goals *would not be feasible given the state of the art as of its submission*. By contrast, Illumina contends that a document that fits in less than a page of its Opening Brief would have enabled construction of a device capable of sequencing the entire human genome in 1989, or a few months thereafter. This supposition is untenable, and especially inappropriate for summary judgment.

16. At his deposition

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17. As Dr. Köster will testify at trial, the SBH Abstract would not enable one of skill in the art to make any device covered by any claim of the '432 patent without undue experimentation. (Exh. 3, Köster Decl. at ¶ 8).

18. There is no guidance regarding visualization of hybridization events, which would be necessary for a functional encoding system. (*Id.*)¶

19. There is no guidance regarding specific synthesis of oligonucleotides to beads. In fact, the preferred system of "20 to 40 marking oligos" would require synthesis of at least 21 different oligonucleotide sequences on a single bead, a process that would be difficult, if not impossible, to decode even today. (*Id.*)

20. There is no discussion of how the "monolayer" of beads would be attached to a surface in a manner that would allow multiple hybridizations. (*Id.*)

21. Additionally, as stated above,

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Although it is true that, under some circumstances, an invention need not have been made to have been enabled by a reference, unsuccessful attempts are evidence of nonenablement. *See AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244-45 (Fed. Cir. 2003).

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24. Moreover, it is simply unrealistic to expect Drs. Crkvenjakov or Drmanac to have revealed their theories at a scientific conference, or through an abstract, in advance of a peer-reviewed publication, in a manner that would allow their competitors to practice their “invention.” Another third-party witness subpoenaed by Illumina, Dr. Richard Sachleben,

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As has been shown, no one – including Drs. Crkvenjakov and Drmanac themselves – “move[d]” significantly *at all* toward implementing the theories discussed in the SBH Abstract.

III. DISPUTED ISSUES OF FACT EXIST REGARDING WHETHER THE SBH ABSTRACT IS A "PRINTED PUBLICATION" FOR PURPOSES OF SECTION 102(B)

25. For a reference to qualify as prior art under § 102(b) it must have been available to the person of skill in the art at the time of the invention. *See In re Cronyn*, 890 F.2d at 1160.

26. Illumina has not produced abstracts from the files of anyone in attendance at either the Santa Fe or Wolf Trap conference other than Dr. Drmanac and Crkvenjakov themselves. Illumina produced no evidence that the abstract booklets were available in any form after the meeting, or were otherwise accessible to persons of skill in the art not in attendance at these conferences. Therefore, Illumina has not shown by clear and convincing evidence that the SBH Abstract is a "printed publication."

27. Further casting doubt on the SBH Abstract's status as a "printed publication" is Dr. Crkvenjakov's testimony that he

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Crkvenjakov's actions

Affymetrix submits that Dr.

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require a credibility determination to authenticate the produced abstracts.

⁴

Until Affymetrix counsel inquired of Dr. Crkvenjakov whether

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~~ther, the poster was presented by Illumina's counsel as anticipatory prior art. (See Exh. 11; Illumina's Supplemental Response to Interrogatory No. 10 at 24, Appendix UU).~~

CONCLUSION

Because substantial disputed material facts exist regarding the adequacy of the disclosure and the validity of the SBH Abstract, Illumina's Motion for Summary Judgment of Invalidity of the Asserted Claims of the '432 Patent should be denied.

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